

Docket No. 2786-0205P

**REMARKS**

The specification has been amended to provide a cross-reference to the previously filed International Application.


The amendment to the claims is merely to delete multiple dependencies and to place the application into better form for examination. Entry of the above amendments is earnestly solicited. An early and favorable first action on the merits is earnestly solicited.

Attached hereto is marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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By   
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Attachment:      VERSION WITH MARKINGS TO SHOW CHANGES MADE

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VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE ABSTRACT OF THE DISCLOSURE:

The Abstract of the Disclosure has been amended as follows:

An ensemble of  $k$  different probing units, for determining by hybridization,  $n$  different target oligonucleotides in an assayed sample. Each of the probing units comprises one or more probe oligonucleotides. The probing nucleotide sequences are capable of hybridizing to target nucleotide sequences, and the probing nucleotide sequences are being capable of hybridizing to target nucleotide sequences, with the probing nucleotide sequences and [of] at least one probing unit being capable of hybridizing to two [or more] different target oligonucleotides in the ensemble.

IN THE CLAIMS:

The claims have been amended as follows:

3. (Amended) An ensemble according to Claim 1[ or 2], characterized in that a plurality of said probing nucleotide sequences can each hybridize to two or more target nucleotide sequences in different target oligonucleotides.

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5. (Amended) An ensemble according to [any one of Claims 1-4]Claim 1, comprising at least two probing units consisting of probe oligonucleotides with probing sequences, which can all hybridize to a target sequence of a single target oligonucleotide.

8. (Amended) An ensemble according to [any one of Claims 1-7]Claim 1, wherein  $k$  is less than about  $10 \times n$ .

13. (Amended) A device comprising a substrate carrying an ensemble of target entities according to [any one of Claims 1-12]Claim 1, with each of the probing units being at a defined location on the substrate.

18. (Amended) A method according to [any one of Claims 15-17]Claim 15, wherein the ensemble of probing units is fixed on a solid substrate at a known coordinate on the substrate.

19. (Amended) A method according to [any one of Claims 15-18]Claim 15, characterized in that the probing units are selected using an optimization model in a computer simulation.

20. (Amended) A method according to Claim 19[ or 20], characterized in that the level of expression of each of the target oligonucleotides in an assayed sample can be calculated by applying the following vectorial equation (1):

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c-Te

(1)

in which

c is a k-dimensional vector of values  $c_1, c_2, \dots, c_k$ , representing the level of hybridization of target oligonucleotides to each of probing units,  $P_1, P_2, \dots, P_k$ , respectively,

e is an n-dimensional vector of values  $(e_1, e_2, \dots, e_j, \dots, e_n)$ , representing the level of expression of each of the target oligonucleotides  $S_1, S_2, \dots, S_n$ , respectively, and

T is an  $n \times k$  matrix of values  $t_{(ij)}$  being the expected level of hybridization of target oligonucleotide  $S_j$  with probing units  $P_i$ .

22. (Amended) A method according to Claim 20[ or 21], wherein the matrix T is a binary matrix.

23. (Amended) A method according to Claim 20[ or 21], wherein the matrix T is a non-binary matrix.

24. (Amended) A method according to [any one of Claims 15-23]Claim 15, wherein said ensemble is that according to [any one of Claims 1-14]Claim 1.

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27. (Amended) A method according to Claim 25[ or 26], characterized in that the vector  $e$  is a sparse vector.

28. (Amended) A method according to [any one of Claims 25-27]Claim 25, wherein the ensemble comprises also reference probing units and level of hybridization of target oligonucleotides to each probing units is compared to the level of hybridization of the target oligonucleotides to the reference probing units.

29. (Amended) A method according to [any one of Claims 25-28]Claim 25, wherein the probing units are immobilized on a substrate, each at a defined coordinate on the substrate.

30. (Amended) A method according to [any one of Claims 25-29]Claim 25, wherein the measured level of target oligonucleotides hybridized to the probing units is compared to the measured level obtained with a control sample.

32. (Amended) A system according to Claim 31, wherein said ensemble is defined in [any one of Claims 2-14]Claim 2.

34. (Amended) A combination according to Claim 33, wherein said ensemble is defined by [any one of Claims 2-14]Claim 2.

(Rev. 11/13/01)